

Amendments to the Specification

Please replace the paragraph at page 12, line 22 through page 13, line 1 with the following amended paragraph:

The SOM is a neural network algorithm widely used for clustering and is well known as an efficient tool for the visualization of multidimensional data (Tamayo, P. *et al.* Interpreting patterns of gene expression with self-organizing maps: methods and application to hematopoietic differentiation, *Proc. Natl. Acad. Sci. U.S.A.* 96, 2907-2912 (1999) and Sultan, M. *et al.* Binary tree-structured vector quantization approach to clustering and visualizing microarray data, *Bioinformatics Suppl* 1, S111-S119 (2002)). The SOM with all the selected 40 genes and/or proteins is carried out according to the method of MATLAB R13 with the SOM toolbox available ~~online in the web site, <http://www.cis.hut.fi/projects/somtoolbox/>~~ (Kohonen, 2001).

Please replace the paragraph at page 20, line 6 through page 21, line 5 with the following amended paragraph:

Gene expression of human primary tumors from glioma patients was examined by high-density oligonucleotide microarrays (U95A array, Affymetrix, Santa Clara, USA, Catalog No. 510137) (Lipshutz, R. L. *et al.* High density synthetic oligonucleotide arrays, *Nat. Genet.* **21**, 20-24 (1999)). For hybridization with oligonucleotides on the chips, the cRNA was fragmented at 95°C for 35 min in a buffer containing 40 mM Tris (Sigma, St. Louis, USA, Catalog No. T1503)-acetic acid (Wako, Osaka, Japan, Catalog No. 017-00256) (pH 8.1), 100 mM potassium acetate (Wako, Osaka, Japan, Catalog No. 160-03175), and 30 mM magnesium acetate (Wako, Osaka, Japan, Catalog No. 130-00095). Hybridization was performed in 200 µl of a buffer containing 0.1 M 2-(N-Morpholino) ethanesulfonic acid (MES) (Sigma, St. Louis, USA, Catalog No. M-3885) (pH 6.7), 1 M NaCl (Nacalai tesque, Kyoto, Japan, Catalog No. 313-20), 0.01% polyoxyethylene(10) octylphenyl ether (Wako, Osaka, Japan, Catalog No. 168-11805), 20 µg herring sperm DNA (Promega, Madison, USA, Catalog No. D181B), 100 µg acetylated bovine serum albumin (Sigma, St. Louis, USA, Catalog No. B-8894), 10 µg of the fragmented cRNA, and biotinylated-control oligonucleotides, biotin-5'-CTGAACGGTAGCATCTTGAC-3' (SEQ ID NO:1; Sawady technology, Tokyo, Japan), at 45°C for 12 hr. After washing the chips with a buffer containing 0.01 M MES (pH 6.7), 0.1 M NaCl, and 0.001% polyoxyethylene(10) octylphenyl ether buffer, the chips were incubated with biotinylated anti-streptavidin antibody (Funakoshi, Tokyo, Japan, Catalog No. BA0500) and stained with streptavidin R-Phycoerythrin (Molecular

Probes, Eugene, USA, Catalog No. S-866) to increase hybridization signals as described in the instruction manual (Affymetrix, Santa Clara, USA). Each pixel level was collected with laser scanner (Affymetrix, Santa Clara, USA) and levels of the expression of each cDNA and reliability (Present/Absent call) were calculated with Affymetrix GeneChip ver. 3.3 and Affymetrix Microarray Suite ver. 4.0 softwares. From these experiments, expression of approximately 11,000 genes in the human primary tumors of glioma patients was determined.

Please replace the paragraph at page 31, line 18 through page 32, line 19 with the following amended paragraph:

Expression of the genes whose expression was statistically significantly different between non-cancerous liver (L0) and pre-cancerous liver (L1), pre-cancerous liver (L1) and well differentiated HCC (G1), well differentiated HCC (G1) and moderately differentiated HCC (G2), moderately differentiated HCC (G2) and poorly differentiated HCC (G3) was analyzed according to the method of MATLAB R13 with the SOM toolbox available ~~online in the web site~~, <http://www.cis.hut.fi/projects/somtoolbox/> (Kohonen, 2001). 40 genes in each comparison between non-cancerous liver (L0) and pre-cancerous liver (L1), pre-cancerous liver (L1) and well differentiated HCC (G1), well differentiated HCC (G1) and moderately differentiated HCC (G2), moderately differentiated HCC (G2) and poorly differentiated HCC (G3) were used. The vectors of neighboring cells were located close to each other in the 155-
[[dimensional]]dimensional gene space (FIG. 3a), where (m, n) indicated the cell located at m-th row and n-th column, NL-XX indicated samples from non-cancerous liver without HCV infection (L0), IL-XX indicated samples from HCV-infected pre-cancerous liver (L1), G1-XXT indicated samples from well differentiated HCC (G1), G2-XXT indicated samples from moderately differentiated HCC (G2), G3-XXT indicated samples from ~~moderately~~ poorly differentiated HCC (G3). The map showed that the samples clearly formed a sigmoid curve in the order of L0, L1, G1, G2, and G3. G2 samples without vessel involvement (blue letters) were located close to G1 samples and G2 samples with vessel involvement (red letters) were located close to G3 samples (FIG. 3a). G2 samples without venous invasion were located close to G1 samples and G2 samples with venous invasion were located close to G3 samples. Thus, the SOM classified G2 samples into two subtypes, *i.e.*, tumor with venous invasion and that without venous invasion, in the stream of dedifferentiation grade. When the distance between the neighboring clusters was shown by colors where red indicated long distance, the red cells in the

- upper area clearly demonstrated that the non-tumorous (non-cancerous and pre-cancerous) liver and HCC samples were relatively far apart in the 155-~~dimensional~~dimensional genes space (FIG. 3b).